REMARKS

Status of the Claims

Claims 1-3, 6-8, 14, 56, and 58 in part and claims 4, 5, and 9-12 in their entirety were examined in the Action mailed October 18, 2006. Claims 13, 15-55, 57, 59, and 60 in their entirety, and claims 1-3, 6-8, 14, 56, and 58 in part, presently stand withdrawn.

Claims 1-5, 7, 9, 14, and 58 are presently amended. Support for the amendment of claims 1 and 58 are found at least in part, for example, at paragraphs 113 and 117, and original claim 4. Claims 2-5, 7, 9, and 14 were amended to correct minor grammatical and typographical errors.

Claims 61-65 are newly added. Support for claims 62-64 is found at least in part, for example, at paragraph 57, and support for claim 65 is found at least in part, for example, at paragraph 59.

A. Objections

Paragraph 34 of the specification and claims 5 and 7 have been amended to correct the minor grammatical and typographical errors objected to in the Action. Applicants sincerely appreciate the notice and respectfully request the objections be withdrawn in light of the amendments.

B. Rejection under 35 USC § 112, ¶ 2

The Action rejected claims 1-12, 14, and 58 under 35 U.S.C. § 112, second paragraph as indefinite. Specifically, the Action alleges that the phrase "a difference in" appearing in independent claim 1 was unclear as to what level of difference in FLJ20174 expression is necessary for diagnosing breast cancer.

Although Applicants believe that claims 1-12, 14, and 58 as examined are fully definite, Applicants have amended claims 1 and 58 in the interest of advancing prosecution. In light of the

amendment that the difference in the expression pattern is an upregulation, Applicants respectfully request that the rejection to all of the claims be withdrawn as moot.

With respect to the rejection of dependent claims 4, 5, and 14, these claims already include the types of additional limitations on the direction and amount of change suggested in the Action. Specifically, dependent claim 4 recites "wherein the difference in the expression pattern is an upregulation of the expression level of CXCL9 or FLJ20174." Dependent claim 5 similarly recites "wherein the difference in the expression pattern is an upregulation of at least two fold over the level of expression of CXCL9 or FLJ20174 nucleic acid." Finally, dependent claim 14 recites "wherein the difference in the expression pattern is an upregulation of the expression level of CXCL9 or FLJ20174 gene product." Because these claims already contained the types of additional limitations urged in the Action, Applicants assume that these claims were rejected as dependent on claim 1, but were otherwise acceptable under 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 USC § 112, ¶ 1

The Action rejects claims 1-12, 14, 56, and 58 under 35 U.S.C. § 112, first paragraph as not being enabled for three reasons: (1) that the claims somehow require distinguishing between breast cancer and another cancer, (2) that the possible number of claimed nucleic acids would require undue experimentation, and (3) that the specification does not provide working examples demonstrating diagnostic significant of any direction or fold change in FLJ20174 expression.

1. The claims do not require distinguishing between breast cancer and another cancer.

As the first basis for the enablement rejection, the Action alleges that the claims are not enabled, because "one could not predictably distinguish between breast cancer and another cancer, such as ovarian cancer, to diagnose breast cancer because it appears that both present with the same marker." Action at 12.

The claims do not require distinguishing between breast cancer and ovarian cancer, but instead are drawn specifically to diagnostic methods that are "indicative of breast or ovarian cancer in the subject." Thus, the claims are not directed to a definitive diagnosis of breast cancer, but rather diagnostic methods that are indicative or breast cancer, and suggest that further analysis of the subject may be warranted. This type of diagnostic method is particularly valuable for identifying early-stage cancer, which typically is more treatable, to help increase long-term survival of the subject.

For example, a blood sample of a subject may be initially analyzed for upregulation in the expression of FLJ20174. If such an upregulation is identified, a tissue such as breast cancer tissue may be obtained from the subject for further analysis (since FLJ20174 is upregulated in breast cancer tissue). One of skill in the art would understand that other analyses, such as radiographic imaging of the breast, can be conducted to confirm diagnosis.

Based on the reasoning presented by the Action, prediction of one specific type of cancer by detecting upregulation of the expression of a particular gene would be enabled only if it occurred for one specific type of cancer, e.g., breast cancer. The Action argues:

> "Thus, undue experimentation would be required to demonstrate that the FLJ20174 RNA expression pattern is solely diagnostic for breast cancer and not for other cancers by, for example, determining the FLJ20174 RNA expression pattern is a larger set of ovarian tumors or by determining the FLJ20174 RNA expression pattern in multiple other tumor types." Action, p. 13.

Such an argument is untenable. Many genes have been shown to be upregulated in more than one cancers. Just because routine subsequent specific tissue testing, imaging, etc. is conducted to confirm diagnosis in no way reduces the fact that prediction of a specific type of cancer by detecting a particular marker is enabled.

As the Action notes, FLJ20174 is overexpressed in 75% of ductal breast carcinomas when compared to normal breast tissue, and the average expression level of FLJ20174 is about 5.5 fold

higher in breast cancer samples than in normal breast tissue. Action at 10-11. Because FLJ20174 is overexpressed in most ductal breast carcinomas, it is a valid marker for diagnosing breast cancer. Applicants thus submit that the claims are fully enabled and request withdrawal of the enablement rejection.

2. Detecting a difference in the expression pattern of FLJ20174 nucleic acid and 30 or more contiguous nucleotides of SEQ ID NO:3 or SEQ ID NO:4 are fully enabled.

As a second basis for the enablement rejection, the Action rejects 1-12, 14, 56, and 58 because the specification does not provide "sufficient guidance to allow one of skill in the art to use the methods claimed because they encompass detecting a whole universe of undefined FLJ20174 nucleic acid molecules." Action, at 15. Similarly, the Action also rejects claims directed to the expression pattern of a nucleic acid comprising 30 or more contiguous nucleotides of SEQ ID NO:3 or SEQ ID NO:4 because those claims involve the use of a "multitude of nucleic acids" not exemplified in the specification. Action, at 16.

With respect to claims directed to FLJ20174 nucleic acids, the specification provides sufficient guidance to allow one of skill in the art to use the claimed methods as claimed. As the Action notes, the specification defines "FLJ20174 nucleic acid sequence" as SEQ ID NO:3 and SEQ ID:4 and homologs, mutations or variants of those sequences found in a subject. This definition, however, does not encompass a "whole universe" of FLJ20174 nucleic acid molecules as the Action contends. The BioTech Life Science Dictionary defines "homologous genes" as "A pair of genes from different but related species which correspond to each other and which are identical or very similar to each other." (http://biotech.icmb.utexas.edu/search/dict-search.html; accessed March 15, 2007). Thus, FLJ20174 nucleic acid homologs are identical or very similar sequences found in other species. Mutations or variants are the various FLJ20174 nucleic acid sequences or alleles found

within a species. As the Action notes, the specification provides two FLJ20174 sequences, SEQ ID NO:3, the wild type isoform of FLJ20174, and SEQ ID NO:4, a splice variant of FLJ20174 that share substantial sequence identity with wild type FLJ20174. Thus, the specification provides an example of a variant FLJ20174, illustrating that mutations and variants, as with homologs, would be easily identifiable by one of skill in the art and show substantial sequence identity to wild type human FLJ20174, as embodied in SEQ ID NO:3.

With respect to claims 9-12, the specification fully enables the claims, which are directed to "detecting the presence in the sample of a nucleic acid comprising 30 or more contiguous nucleotides of SEQ ID NO:1, SEQ ID NO:3 or SEQ ID NO:4." First, the specification provides the nucleotide sequences of SEQ ID NO:3 and SEQ ID NO:4. One of skill in the art could easily identify any nucleotide sequence comprising 30 or more contiguous nucleotides of SEQ ID NO:3 or SEQ ID NO:4.

Second, the Action seems to allege that sequences comprising at least 30 contiguous nucleic acids of SEQ ID NO:3 or SEQ ID NO:4 occur commonly among expressed genes and would thus fail to exhibit the diagnostic expression pattern of the entire SEQ ID NO:3 or SEQ ID NO:4. Action, at 16. This, however, is not the case. As discussed in the specification at page 17, probes or primers which are only a portion of a larger nucleotide sequence are routinely used for detection of nucleotide sequences. For example, Example 2 in the specification uses pairs of 20 nucleotide long primers for PCR amplification of specific nucleotide sequences. Although base usage is not strictly random and independent, the odds of a sequence of 30 contiguous nucleotides of SEQ ID NO:3 occurring randomly in a genome is roughly 1 in 4^{30} bases (1 in 1.15×10^{18} or 1 in 1.15 quintillian).

Because FLJ20174 nucleic acids would share substantial identity with the disclosed sequences, Applicants submit that there would not be a "multitude" of possible FLJ20174 nucleic

acids requiring undue experimentation. Similarly, because methods utilizing portions of nucleic acid sequences are routinely used in the art and sequences of 30 or more contiguous nucleotides would be expected to be very specific, one of skill in the art would not be forced into undue experimentation in order to practice the claimed invention. Consequently, Applicants respectfully request removal of the rejection.

3. Enablement of the diagnostically significant of any direction or fold change in FLJ20174 expression.

As the final basis for its enablement rejection, the Action rejected claims 1-12, 14, 56, and 58, alleging the specification did not provide working examples to demonstrate that a difference, as recited in claim 1, in the expression pattern of FLJ20174 between two tissue samples, was diagnostically significant. Action, at 19.

Although Applicants believe the rejected claims were fully enabled, in the interest of advancing prosecution, Applicants have amended claims 1 and 58 such that the difference in the expression pattern is upregulation. Applicants respectfully request reconsideration of the rejection in light of the amendments.

As with the § 112, second paragraph, rejection discussed above, Applicants note that dependent claims 4, 5, and 14 already incorporated the limitations suggested in the Action and were thus rejected because they depended from independent claim 1, but were otherwise fully enabled with respect to this basis of the enablement rejection.

D. Rejection under 35 U.S.C. § 112, ¶ 1

Finally, the Action rejected claims 1-12, 14, 56 and 58 as lacking adequate written description. Action, at 19. Specifically, the Action alleges that Applicants have not provided an adequate description of "any FLJ20174 nucleic acids whose difference in expression diagnoses

breast cancer" or of "a nucleic acid comprising 30 or more contiguous nucleotides SEQ ID NO:3 or SEQ ID NO:4 that is useful for diagnosing breast cancer." Action, at 21, 25.

This rejection appears to be related to the enablement rejections discussed sections C.1, C.2, and C.3 above. To the extent that this is the case, Applicants request reconsideration of the rejection in light of the arguments made above. Additionally, Applicants note they have provided SEQ ID NO:3 and SEQ ID NO:4 and have provided working examples demonstrating changes in expression of SEQ ID NO:3 and SEQ ID NO:4 as diagnostic for cancer. Moreover, by disclosing the entire SEQ ID NO:3 and SEQ ID NO:4, Applicants have provided all possible nucleic acids comprising 30 or more contiguous nucleotides of SEQ ID NO:3 or SEQ ID NO:4 and placed them fully in possession of one of skill in the art. In addition, as already discussed by Applicants herein, the odds of such a 30 contiguous nucleotide sequence occurring randomly is 1 in 1.5×10^{18}. To the extent that this rejection is not related to the enablement rejection above, Applicants request clarification of the rejection.

CONCLUSION

In summary, Applicant's believe that the claims are in condition for allowance. Such favorable action is respectfully requested. If the Examiner has any questions or comments regarding any issue associated with this application a telephone call to the undersigned representative at 512.542.8619 is welcome.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

Tracey B. Davies
Registration. No. 44,644
Attorney for Applicant

VINSON & ELKINS L.L.P.
First City Tower
1001 Fannin Street, Suite 2300
Houston, Texas 77002-6760
Ph: 512.542.8619
Fax 512.236.3215

Date: March 20, 2007

Austin 811808v.1